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Enantioselective Synthesis of a Dual Orexin Receptor Antagonist  

Synthesis of Suvorexant

**Significance:** Orexins A and B are excitatory neuropeptides that stimulate wakefulness. Suvorexant is a dual orexin receptor antagonist that is in phase III clinical trials for the treatment of insomnia. The key step in the asymmetric synthesis depicted is a tandem enzymatic transamination–annulation sequence (F → G → H).

**Comment:** A previous synthesis of suvorexant (N. A. Strotman et al. J. Am. Chem. Soc. 2011, 133, 8362) involved an asymmetric Ru-catalyzed reductive amination in the construction of the diazepane ring. The present route benefits from the circumvention of transition-metal catalysis and dichloromethane as solvent.